Melanocortins protect cultured dorsal root ganglia against the toxic effects of cytostatic drugs.

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Certain cytostatics have a polyneuropathy as dose-limiting side effect. For example, cisplatin, a powerful cytostatic used in ovarian and testicular cancer and taxol, another potent cytostatic, can cause a sensory neuropathy, which may lead to loss of the vibratory sense which eventually results in severe disability. In vivo, a trial has shown that co-treatment with ORG2766, a man-made analog of $ACTH_{4-9}$, can ameliorate the loss in sense of vibration, but also lead to less signs and symptoms as scored by patients themselves. We wanted to develop an *in vitro* model to study cisplatin- and taxol-induced neuronal damage and see whether melanocortins could ameliorate the toxic action of cisplatin and taxol *in vitro* as ORG2766 has shown to do *in vivo*.

We cultured ED12 chick dorsal root ganglia (DRG) in a semi-solid medium and treated them with cisplatin (0.1 - 20 µg/ml) or taxol (0.01 - 20 µg/ml) with and without αMSH or ORG2766. Axonal outgrowth was evaluated daily by measuring the mean length (l_{av}) and growth rate (r_g) of neurites and, later, also with a computer-assisted image analysis system. The presence of cisplatin (10 µg/ml = 33 µM) resulted in a substantial reduction in r_g (from 150 to 85 µm/day) and in l_{av} (610 vs 340 µm at day 4). In cultures treated with cisplatin + αMSH (10nM), a significant improvement of axonal outgrowth was observed: the initial r_g was 53% higher and the l_{av} at day 4 was 455 µm. Taxol also reduced spontaneous outgrowth at lower concentrations than cisplatin. Again, ORG2766 and αMSH appeared capable of restoring outgrowth. We conclude that the melanocortins αMSH and ORG2766 have a neuroprotective effect *in vitro* which can be easily quantified in the sewmi-solid culture system.

Source: https://www.industrydocuments.ucsf.edu/docs/ryfb0000